Journal of Spine
ISSN: 2165-7939

Reyes-Sánchez, J Spine 2016, 5:2
DOI: 10.4172/2165-7939.1000295

Research Article Open Access

Usefulness of Computed Tomography (CT)-Guided Biopsy for Etiological Diagnosis of Vertebral Destruction Syndrome

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Abstract

Purpose: It has been observed to biopsy directed by computerized axial tomography as axis for the diagnosis of vertebral destruction syndrome VDS. Evaluate the usefulness of CT-guided biopsy to determine the etiology of VDS.

Method: Cross-sectional, analytical study of diagnostic tests, which took place in individuals of any age who were admitted with a diagnosis of syndrome of vertebral destruction, attended for the first time. The sample size consisted of 91 patients; computerized axial tomography-guided biopsy was performed. We compared the results of the biopsy between two pathologists from different institution.

Results: Definitive histological findings were grouped into 7 categories: osteomyelitis (15.3%), tumors (38.46%), metastasis (37.36%), normal tissue (3.29%), inflammation (2.19%), and showing inadequate 0%, Pott's disease (3.29%). According to the values of Z obtained by test of 2 proportions, with a n = 91, p = 0.05, the critical value of Z, two-tailed, was from 1.966 (±); they found no significant difference between the results reported by 2 different pathology services in vertebral biopsy guided by CT in Vertebral destruction syndrome; determining that this part of the process is a counselor on a 96.7% and final by 79%.

Conclusion: Percutaneous biopsy guided by tomography is an essential tool for the diagnosis of the syndrome of vertebral destruction approach and the ability to get diagnostics in the 96.7% indicates that it is a fundamental in the study of this syndrome.

Keywords: Spinal infection; Spinal neoplasms; Spinal tuberculosis; Osteoporosis spine; Image-guided biopsy; Vertebral destruction

Introduction

Vertebral destruction syndrome (VDS) is a disease with multiple etiologies characterized by changes in the structure and ultrastructure in the bone of the spine resulting in deformity as well as increase in surrounding volume in one or more vertebral bodies. VDS is accompanied by pain and functional disability due to mechanical and neurological changes [1,2]. Diagnosis of the set of pathologies originating from VDS is related with laboratory data, imaging tests and specific findings for each disease according to imaging studies [3-21]. Studies report that biopsy is the most important procedure for the etiological diagnosis of VDS [22-28]. However, Rosales et al. [1] studied the usefulness of fluoroscopy-guided percutaneous transpedicular biopsy for diagnosis of VDS in 20 patients. Specific histological diagnosis was only able to be made in 55% of the patients, demonstrating little usefulness, even though numbers of the variables and case series were in agreement with the majority of other series published.

In 2007, Alpízar et al. [2] proposed systematization with a series of tests that included laboratory tests, imaging tests and percutaneous biopsy to arrive at the etiological diagnosis of VDS. One hundred and five patients were included in that study with different pathologies. Patients were grouped according to three categories (infections, tumors, and metabolic disorders). Systematization and clinical files were used for the studies. As a general conclusion, there was no agreement with regard to the international medical literature according to the sensitivity and specificity results of the diagnostic studies. Therefore, a new simplified systematization process was proposed from the results obtained in the mentioned protocol using the studies with greater sensitivity and specificity, with the aim of reducing costs without affecting and even improving effectiveness of the diagnostic methods.

A preliminary study was carried out in 20 patients in whom ten different laboratory tests and imaging tests were performed as well as histopathological study of the biopsy in order to arrive at the etiological diagnosis of VDS. In this pilot study, description of the new systematization of studies proposed by Alpizar in 2008 was made with the intent of optimizing hospital resources and, at the same time, to make the diagnosis of VDS more effective with results similar to those in the series mentioned [19].

Computed tomography (CT)-guided biopsy achieves the diagnosis with a certainty of up to 95% [25,27]. In another publication, a review of two different pathologists from different institutions found no significant differences between the studies reported by the two pathology services according to the z-values obtained by means of the comparison test of two proportions. It was determined that this part of the process is reliable and useful in 90% of patients [28].

After completion of the pilot study [28] we decided to expand the sample in order to confirm the viability of the idea in the diagnosis of this common pathology in Mexico. The main goal of this study is to evaluate the usefulness of CT-guided biopsy to determine the etiology of VDS, with the specific objectives of studying diagnostic accuracy, sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) for CT-guided biopsy and to compare the biopsy interpretation with the study

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Received September 25, 2015; **Accepted** March 21, 2016; **Published** March 23, 2016

Citation: Reyes-Sánchez AA, Obil-Chavarría C, Sánchez-Bringas G, Lara-Padilla E (2016) Usefulness of Computed Tomography (CT)-Guided Biopsy for Etiological Diagnosis of Vertebral Destruction Syndrome. J Spine 5: 295. doi:10.4172/2165-7939.1000295

of the definitive specimen. We propose that the use of a CT-guided biopsy improves the ability to arrive at a diagnosis in above 95% of patients with vertebral destruction syndrome.

Materials and Methods

Type of study

We carried out a cross-sectional analytical study.

Type of sampling

A consecutive census sampling was done with all diagnostic tests performed from March 1, 2011 to October 31, 2012.

Study Subjects

The study population was a consecutive series of participants defined by the selection criteria. Subjects of any age and both genders were included and they had not received prior treatment. Subjects were admitted to the Service of Spinal Surgery of our hospital with an initial diagnosis of VDS in the thoracic and lumbar regions. Exclusion criteria were patients who did not consent to undergo the proposed diagnostic studies or those who, due to medical circumstance, were unable to undergo some of the proposed diagnostic procedures.

Procedures

For the present study, the *independent variable* was CT-guided biopsy. The *dependent variable* was the histopathological diagnosis obtained from the biopsy. The patient was initially identified on continuous admission or hospital admission with the diagnosis of VDS. The following information was obtained for each individual: age, gender, affected segment, affected vertebra, number of vertebra affected, hemoglobin, hematocrit, leukocytes, glucose, urea, creatinine, coagulation time, general urinalysis, Bence-Jones protein, HIV status, polymerase chain reaction for tuberculosis (TB), skull x-rays, nuclear magnetic resonance (NMR), bone scan, and level of pain after biopsy procedure noted on the systematization sheet for the service for this pathology, which also includes CT-guided biopsy during the patient's hospitalization. When the final biopsy result was obtained, a consensus meeting including medical experts in the field was held to confirm the final diagnosis and the probability for subsequent definitive treatment. In cases where the patient was subjected to a surgical procedure consisting of debridement, the final diagnostic result was corroborated.

Possible diagnostic classifications were as follows: benign tumor, malignant tumor, metastasis, infection, Pott Diseases, metabolic disorder, insufficient specimen and/or normal tissue. To ensure reproducibility of the test, three steps were carried out: 1) patient preparation, 2) surgeon training for performing the biopsy, and 3) description of the technique.

No specific preparation was necessary for the procedure; however, for ease and patient safety, fasting was indicated for at least 6 h prior to the study. Patients were informed of the need to be placed in prone decubitus position and that the test would be performed under local anesthesia. Some discomfort during the injection and during the procedure was expected due to the position. The study was done using a team of physicians and technicians from the CT service; however, the spine surgeon involved in the study determined the initial position of the needle required and administration of the local anesthetic in possible trajectory of the puncture.

For transpedicular biopsy, a Jamshidi needle (Cardinal Health Co., Dublin, OH, USA) with a 5-mm diameter and 15 cm length was used. During insertion of the needle, tomography films were taken to verify the adequate direction and depth of the needle so as to avoid damage to nerve structures. Once the most representative site of the lesion was reached, the trephine was removed, lesion contents were aspirated and the needle sheath was removed simultaneously exerting negative pressure to obtain samples of the soft tissue, liquid and solid material (bone tissue). Once the Jamshidi needle was removed, tomography film was obtained of the puncture site to ensure no active bleeding. The solid tissue sample obtained (bone or soft tissue) was transported to the Pathology Department. The fluid sample was placed in a Stuart transport medium and transported to the microbiology laboratory for analysis.

The resulting slide from the CT-guided biopsy was interpreted by two different pathologists: the first pathologist affiliated with the hospital where the specimen was obtained and the second pathologist from outside our institution. Results of the biopsy were validated with the final diagnosis from the histopathological study of the surgical specimen or definitive diagnosis according to correlation studies, having been verified and established by the treating physician.

Statistical Analysis

A descriptive analysis was carried out for continuous quantitative variables using measures of central tendency (mean, median, and mode) and dispersion (standard deviation, maximum values, minimum values and ranges). Categorical data were described with percentages and frequencies.

Comparison with magnetic resonance imaging with the contrast enhancement (MRI) was used because it was proven to be the gold standard, using the complete sample of patients in carrying out the analysis. A database was constructed. For "tumor" classification, absence of disease was coded as "0" (for patients with diagnosis of a disease other than tumor) and as "1" as tumor according to the MRI results as a standard of reference or true positives. True negatives were those patients without tumor according to MRI or biopsy. False positives were those with MRI without tumor and positive biopsy, whereas false negatives were assigned to those with MRI evidence of disease and negative biopsy. Similarly, we coded the other two categories as "infectious" and "osteoporosis". Contingency tables (2 x 2) were constructed as well as tables for the serial analysis only for cases from the "infectious" category. Data from the tables were analyzed using EpiDat v.3.1 software to obtain values for sensitivity, specificity, PPV and NPV, among other indicators for test performance, using as a reference the MRI values [29,30]. For analysis of the characteristics and properties of the diagnostic test, we used 2 x 2 tables. Results of the pathologist were analyzed with the comparison test of two proportions. Statistical packages SPSS v.17 and Epidat were used; $p < 0.05$ was accepted as statistically significant. Confidence interval (CI) was calculated for proportions with the following formula using a confidence level of $p = 0.05$:

$$\left[\left[p - z_{\frac{\alpha}{2}}\left(\sqrt{\frac{pq}{n}}\right)\right\langle p\left\langle p + z_{\frac{\alpha}{2}}\left(\left(\sqrt{\frac{pq}{n}}\right)\right)\right)\right]$$

Results

Of a total of 105 patients, 14 patients were eliminated due to incomplete clinical files. The final sample was n = 91 patients; 47.25% (n = 43) were females and 52.7% (n = 48) males. Mean age was 53 years (female = 51.4, male = 56.5) with a maximum age of 88 years (range 8-88 years) (Figure 1). For heigh the average was 1.68 cm for males and 1.62 cm for females. The most affected vertebral segment was the

lumbar segment (62.64%) followed by the thoracic segment (31.87%) and the third most affected was the cervical segment (2.2%) (Table 1). Involvement of only one segment was found in 85.7%, whereas two-level involvement was found in 13.2% and three or more levels in 1.1%. Definitive histological results were grouped into seven categories (Table 2): osteomyelitis (microorganisms and inflamamatory cell response in the biopsy) in seven patients (15.38%), tumors 35 patients (38.46%), metastasis 34 patients (37.36%), normal tissue 3/91 patients

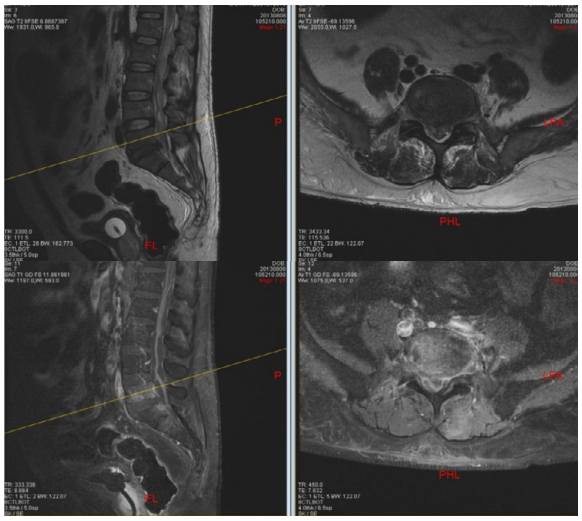

Figure 1: **Simple and contrast enhanced MRI in sagittal and axial views.** T1 hypointense, T2 hyperintense and contrast enhanced soft tissue lesion involving L5-S1 vertebral disc, L5 and S1 vertebrae and paravertebral tissue extension with a left psoas abscess. **CT-guided biopsy** reported chronic and acute osteomyelitis.

Variables	n= 91	%
Gender		
Male	48	52.7
Female	43	47.25
Affected Vertebral Segment		
Cervical	2	2.20
Toracic	29	31.87
Lumbar	57	62.64
Sacro	1	1.10
Cervico-toracic	1	1.10
Toraco-lumbar	1	1.10

Table 1: Demographic and clinical data.

Cathegory	Pathologist #1	Pathologist #2	Z Value*	Definitive Diagnosis**	%
Osteomielitis	14	12	0.423	14	15.38
Tumor	36	39	-0.451	35 (y)	38.46
Metastasis	33	27	0.946	34 (y)	37.36
Normal Tissue	3	2	0.453	3	3.29
Inflammation	2	8	-1.951	2	2.19
Inadequate specimen	0	0	0	0	0
Pott Disease	3	3	0	3 (y)	3.29

N= 91, $p = 0.05$.
*Critic value of Z was 1.966 (±).
**definitive diagnosis was established as: (a) expert opinion (oncologist in the case of malignancy, infectious disease specialist in the case of infection), (b) microbiology culture, or (c) overall interpretation of the remaining studies established in the previously reported diagnostic protocol, and (d) result of the open biopsy, and the total is equal 79.09%.

Table 2: Comparative analysis of pathology samples.

Diagnosis	Sensitivity Value (95% CI)	Specificity Value (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Tumor	85.45% (66.9–105.35)	99.01% (88.89–109.85)	98.07% (76.35–117.71)	92.08% (79.77–102.91)
Infection	70.49% (49.30–94.96)	94.17% (86.78–100)	83.88% (63.96–100)	88.114% (76.89–98.44)
Parallel test with culture	96.67% (88.58–100)	87.72% (78.32-97.12)	80.56% (66.24–94.87)	98.04% (93.25–100)
Parallel test with PCR-TB	92.71% (74.96–113.96)	85.65% (75.46–94.69)	73.55% (55.3–90.34)	96.46% (86.36–105.03)
Osteoporosis	85.71% (52.65–100)	92.50% (86.10–98.9)	50% (17.54–82.46)	98.67% (95.4–100)

* Sensitivity, Specificity, Positive predictive value (PPV) and Negative predictive value (NPV).

Table 3. Diagnostic test values of the CT-guided biopsy for the diagnosis of vertebral tumors, infections and metabolic diseases.

(3.29%), inflammation (mainly acute and chronic cellular response in the biopsy) two patients (2.19%), inadequate sample 0%, and Pott's disease three patients (3.29%). We did not have nondiagnostic biopsies reported by the pathologists. According to the distribution of the population, z-test was used to compare proportions (n = 91, p = 0.05). No significant difference was found between the results reported by two different pathology services in CT-guided vertebral biopsy in VDS, determining that this part of the process is informative in 96.7% and definitive in 79%.

After preparing the corresponding 2 x 2 tables, for the "tumor" pathology an adjusted sensitivity of 85.45%, specificity 99.01%, validity index of 94% (95% CI 83.16-103.32), PPV 98.07%, NPV 92.08%, and disease prevalence of 36.94% (95% CI 25.51-50.92) was obtained.

For the "infectious" pathology, CT-guided transpedicular percutaneous biopsy as a simple test reported a sensitivity of 70.49%, specificity of 94.17%, validity index of 87.04% (95% CI 77.64-96.13), PPV 83.88%, NPV 88.114% and disease prevalence of 30.09% (95% CI 18.34-41.85).

As a parallel test with culture, sensitivity of 96.67%, specificity of 87.72%, validity index 90.80% (95% CI 84.16-97.87), PPV 80.56%, NPV 98.04% and disease prevalence of 34.48% (95% CI 23.92-45.05) was obtained.

Biopsy performed in parallel with polymerase chain reaction (PCR) for TB reported a sensitivity of 92.71%, specificity 85.65%, validity index 87.77% (95% CI 78.53-96.13), PPV 73.55%, NPV 96.46% and disease prevalence of 30.09% (95% CI 18.34-41.85).

For osteoporosis, sensitivity was reported of 85.71%, specificity 92.50%, validity index of 91.95% (95% CI 85.66-98.24), PPV 50%, NPV 98.67% and disease prevalence of 8.05% (95% CI 1.76-14.34). (Table 3).

In regard to comparison with the definitive diagnosis of the specimen, this was not possible. In 75% of the cases, the final diagnosis was tumor or metastasis, with the patient being sent to the appropriate institution for definitive treatment. Information on outcome of the progress of the patient is unknown to us. On the other hand, 15% of the cases were related to bacterial infections. Treatment was carried out with specific antibiotics. The final surgery was not done due to debridement but for structural correction. Corroboration of the diagnosis was evidenced by the favorable evolution of the patient and negative results according to the definitive histopathological study. The definitive specimens were concordant with the biopsy in only 3% of cases diagnosed with Pott's disease. In all cases there were no complications with regard to the biopsy procedure.

Discussion

Diagnosis of VDS tends to be uncomplicated because patients seek consultation with specific symptoms, which may involve a neurological lesion. Images from simple x-rays demonstrate the presence of vertebral structural problems even when corroborated with an MRI; however, etiology of the pathology is difficult to discern [2,31].

Systematization for the diagnosis of VDS is essential. Costs associated with its diagnosis can be high due to lack of a plan of order owing to its various origins [28]. There may even be a genetic component that may change its focus [32-38]. Diagnosis according to MRI is not always simple. Images may be shown that confuse the etiologies from infection to tumor and vice versa or even make difficult determining the type of infection (bacilli, bacterial or fungal) [16,29,30].

The study by Alpizar et al. [2] reports that MRI has an average sensitivity of 54.4% and specificity of 94%. Nonetheless, for bone metastasis, bone scan surpassed other tests with a sensitivity of 75% and a specificity of 96%, increasing the sensitivity to 80% once the combination with MRI is carried out. For this reason, in our study and with this history, the test with which we compared specificity and predictive value was MRI, obtaining an adjusted sensitivity for tumor pathology of 85.45%, specificity 99.01% and disease prevalence 36.94%. For infectious pathology, we obtained sensitivity of 70.49%, specificity of 94.17%, and disease prevalence of 30.09%. For TB, combining the biopsy in parallel with polymerase chain reaction, sensitivity of 92.71%, specificity of 85.65% and disease prevalence of 30.09% (95% CI 18.34-41.85) were reported. For osteoporosis, sensitivity of 85.71%, specificity of 92.50%, and disease prevalence of 8.05% were reported. Predictive values fluctuated from 50-98% depending on the disease and NPV was always ~98%. With these results we can affirm that CT-guided percutaneous biopsy should be considered as the gold standard for the etiological diagnosis of VDS and, even more so, if Figures 2 and 3 reported in the international literature support our results.

Division into four parts did not produce significantly higher values in the results of the "normal sample" (3.29%), with a diagnosis in 96.7% of the cases. This is comparable to rates reported in large case series (3). However, considering primary tumors, metastases and Pott's disease as the only diagnoses that provide definitive etiology, diagnostic certainty of this study corresponds to 79% [27,28,37,38].

In our sample, definitive diagnosis was established as: a) expert opinion (oncologist in the case of malignancy, infectious disease specialist in the case of infection), b) microbiology culture, or c) overall interpretation of the remaining studies established in the previously reported diagnostic protocol, and d) result of the open biopsy. Of the results obtained, ten were able to be corroborated [Pott's disease (3 patients), primary tumor (6 patients) and metastatic tumor (1 patient)] by means of definitive histopathological study with a specimen obtained during the surgical procedure. For the three cases reported as a normal study, diagnosis of fracture secondary to osteoporosis was able to be made when densitometry was done.

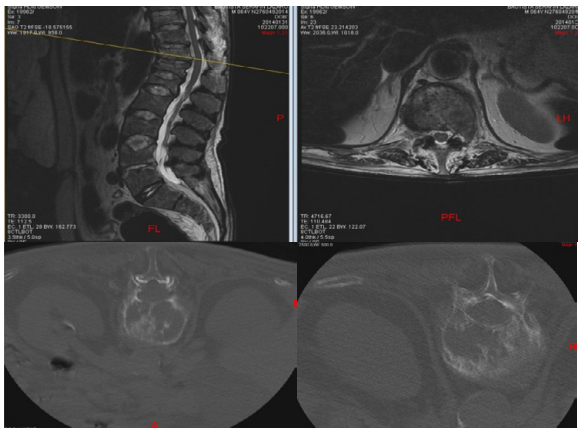

Figure 2: Simple MRI. Sagittal and Axial views. Diffuse infiltration of multiple vertebrae with discrete hypointense T1, discrete hyperintense T2 and no T2 Fat-sat enhancement, related to tumoral etiology. T9 to L1 vertebral collapse that conditions thoracolumbar xifosis. **CT-guided biopsy** reported multiple myeloma.

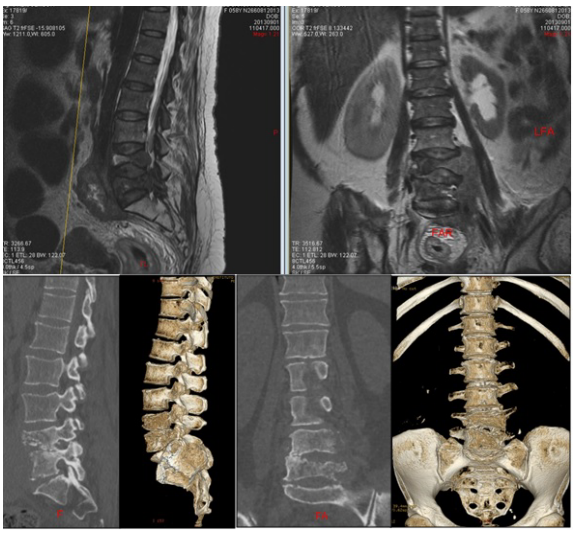

Figure 3: Simple MRI . Sagittal and Coronal views. Infiltrative process involving L4 and L5 vertebrae which are collapsed in 70-80%. The infiltration extends as a 66x35mm prevertebral tumor with soft tissue intensity and heterogenous aspect that surrounds great abdominal vessels and left ureter causing left hydronephrosis. Multiple hyperintense punctate lesions in both iliac crests, of lytical aspect. These images suggest tumoral infiltration, probably metastatic. **CT-guided biopsy** reported keratinizing squamous cell carcinoma metastasis.

According to the z-values obtained with the comparison test of two proportions, no significant difference was found between the results reported by the two different pathology services in CT-guided vertebral biopsies in VDS, with the determination that this process is suggestive in 96.7% and definitive in 79%.

A limitation of our study is that no reproducibility tests were done; however, this phenomenon could be inferred due to the diagnosis in 79% of cases with diagnostic accuracy due to biopsy and to the fact that there were no complications as the result of the biopsy, even after 48 h. Likewise, motivated by the characteristics of the design, it was not possible to determine the inter- and intra-observer correlation. Although observers blindly evaluated the specimens from the same patient, they did not evaluate the same slides or portions of the biopsies. The important value of this paper is the confirmation of high significance of the biopsy and no significant difference between the results reported by two pathologists.

Conclusion

CT-guided percutaneous biopsy is a fundamental tool for the diagnostic approach of VDS. The ability to arrive at a diagnosis in 96.7% of patients indicates that it is central in the study of this syndrome. It validates the CT guided vertebral biopsy as a reliable diagnostic tool in establishing correct diagnosis. Systematization with studies allows obtaining 100% diagnostic accuracy by guiding the diagnosis when it cannot be done with only the biopsy.

Acknowledgments

These paper has the PhD Thesis, of Alejandro Reyes-Sánchez in the Medicine school of Instituto Politecnico Nacional.

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